

Remarks

Sequence Listing

A statement indicating that the paper copy and CRF of the Sequence Listing filed 1/18/05 do not include new matter is enclosed herewith.

Specification

The specification is objected to as failing to provide proper antecedent basis for claim 34. Claim 34, which was drawn to the transgenic nematode of claim 1, wherein the gene is *C. elegans vap-2* has been canceled. Applicants had indicated to the undersigned prior to the submission of the Office Action Response filed 1/18/05 that this claim should be canceled. Its inclusion in the previous Office Action Response was inadvertent.

Rejections under 35 U.S.C. § 112

Claims 1-13, 15-35, and 46-53 remain rejected and claims 106-142 are rejected under 35 U.S.C. § 112, as failing to comply with the written description requirement. Claims 15-23, 26-45, 110-114, 119-121, 125-130, and 137-142 have been canceled, therefore the following remarks concern the remaining claims, as amended.

The Examiner states that new matter has been introduced by the previous amendment and continues to maintain that the specification does not adequately describe a genus of regulatory elements that would direct expression as recited in the claims. While not agreeing with the Examiner's position, Claim 1 has been amended to recite an embodiment in which the transgene comprises a regulatory element of the *C. elegans vap-1* gene and to recite that the detectable marker is expressed in amphid sheath cells, which the Examiner acknowledges as being adequately described. Withdrawal of the rejection of claim 1 and the remaining claims dependent therefrom is respectfully requested.

The Examiner states with respect to claim 46 that "the regulatory region...remains generic with respect to the nematode from which the region is isolated and with respect to whether the endogenous gene from which the regulatory element is derived is normally expressed in a pharyngeal gland cell or amphid sheath cell of *C. elegans* or another nematode." Applicants respectfully submit that step (c) of claim 46 specifies that the regulatory region is

from a *C. elegans* gene rather than being generic with respect to the nematode from which the regulatory region is isolated. Claim 46, step(b), has been amended to indicate that the *C. elegans* homolog from which the regulatory region is isolated is a *C. elegans* secretory product.

Applicants note that the Examiner has acknowledged that embodiments in which the regulatory region is from a gene encoding a secreted product from *C. elegans* are supported by the specification at paragraph 73, Examples 4, 8, and 9, and original claims 15-18. The amendment is further supported at paragraphs 103 and 104.

Applicants note that the Examiner has not asserted any specific reason for rejecting claim 46 for lack of written description other than that the regulatory region from which the endogenous gene is derived is generic. This ground has been addressed with the instant amendment. Applicants point out that the specification describes methods for selecting a parasitic nematode secretory protein; methods for identifying a *C. elegans* homolog of a parasitic nematode secretory protein; methods for determining whether a protein is a *C. elegans* secretory product; methods to determine which cell(s) express the *C. elegans* homolog of a parasitic nematode secretory protein, e.g., to determine whether the homolog is expressed by *C. elegans* secretory cells; methods for identifying a nucleic acid sequence comprising a regulatory region of a *C. elegans* gene encoding the *C. elegans* homolog; and methods for generating a transgenic *C. elegans* nematode, wherein cells of the transgenic nematode comprise a nucleic acid sequence including the identified regulatory region operably linked to a nucleic acid sequence encoding a detectable marker, wherein the detectable marker is expressed in a pharyngeal gland cell or amphid sheath cell. The Examiner has acknowledged that , “one may presume that regulatory elements from other *C. elegans* genes encoding secretory products (that, *sic*) would direct expression in a pharyngeal gland cell or amphid sheath cell exist, and the specification describes methods by which one could identify endogenous secretory products that are secreted from a pharyngeal gland cell or amphid sheath cell in *C. elegans* or the analogous organs in other nematodes.” (office action of 4/6/05, page 5). With respect to step (c), the Examiner has acknowledged that the specification teaches, “a method for obtaining...regulatory elements for use in making the claimed invention” (office action mailed 4/6/05, p. 12, see also p. 15, referring to the fact that Applicant’s disclosure teaches a potential method for isolating regulatory elements required by the claims). Accordingly, withdrawal of the rejection of claim 46 and claims dependent therefrom is respectfully requested.

The Examiner states that claim 106 incorporates new matter since it is generic to the cell in which the polynucleotide is expressed while original claim 100 limited the expression specifically to amphid sheath cells. Applicants submit that the instant specification generally teaches the creation of a transgenic nematode, wherein the transgene comprises a *vap-1* regulatory region operably linked to a first polynucleotide. The fact that Applicants examined the expression pattern of the transgene in a particular embodiment of the invention and found that the transgene was expressed in amphid sheath cells should in no way require Applicants to limit their claim to embodiments in which expression occurs in amphid sheath cells. However, in the interests of furthering prosecution, claim 106 has been amended to recite that the transgene is expressed in amphid sheath cells. Applicants point out that neither claim 100, nor amended claim 106, limits expression of the transgene to amphid sheath cells. They merely recite that expression of the transgene occurs in amphid sheath cells. Withdrawal of the rejection of claim 106 and claims dependent therefrom is respectfully requested.

Claims 115 stands rejected on the ground that the recitation “or both” is new matter since the specification does not explicitly describe a secretory protein expressed in both glands. Claim 115 has been amended to remove the recitation, “or both”. Claim 124 has also been amended to remove the recitation “or both”. The claims now recite that the secretory protein is expressed in a pharyngeal gland cell or an amphidial gland cell (claim 115) or that the secretory protein that is expressed in a pharyngeal gland cell or an amphid sheath cell (claim 124), consistent with the terminology used in the specification. However, Applicants point out that the claims still encompass situations in which a protein is expressed in both pharyngeal gland cells and amphidial gland cells (claim 115) and situations in which the protein is expressed in both pharyngeal gland cells and amphid sheath cells (claim 124).

Claims 115-118 are rejected on the ground that they only require that the regulatory element comprise a sequence of unspecified length from the region bounded by the start codon and a point 10/8/6 kb upstream of the start codon, whereas the Examiner asserts that the specification teaches that the transgene will include all of the genomic DNA from the start codon and upstream sequences extending from 2, 4, 6 kb, etc. Claim 115 has been amended to recite that cells of the transgenic nematode comprise a DNA element encoding a detectable marker operably linked to a regulatory sequence of the gene that encodes the *C. elegans* homolog rather than reciting an embodiment in which the regulatory element is found within a particular position range. Support for the amendment is found at p. 53, lines 2-13 and at p. 55, lines 29-30

(paragraphs 121-122 and 126). Claims 116-118 and 122-123 have been amended to recite methods for generating a transgenic nematode rather than being drawn to transgenic nematodes. Support for the amendment is found at p. 55, line 29 - p. 56, line 17 (paragraphs 126 and 127). Applicants submit that the claims are fully described in the specification and note that the Examiner has acknowledged that the specification describes methods for identifying secretory proteins and regulatory elements for use in making the claimed invention. Withdrawal of the rejection is respectfully requested.

Claim 124 has been amended to recite that the transgene comprises a DNA element that encodes a detectable marker operably linked to a regulatory sequence of the gene that encodes the *C. elegans* secretory protein. Claims 125-128 have been amended to recite methods for generating transgenic nematode rather than being drawn to transgenic nematodes. Support for these claims is found as described above for claims dependent on claim 115. Withdrawal of the rejection is respectfully requested.

Claims 1-13, 15-35, 46-53, 114-119, and 122-129 stand rejected under 35 U.S.C. § 112, first paragraph, on the ground that the claims contain subject matter that was not described in the specification in such a way as to convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended to recite that a transgenic *C. elegans* in which the transgene comprises a regulatory element of the *C. elegans vap-1* gene, which the Examiner acknowledges as being enabled. Withdrawal of the rejection of claim 1 and claims dependent therefrom is respectfully requested.

Claim 46 has been amended as described above, to recite that the *C. elegans* homolog is a secreted product of *C. elegans*, which the Examiner acknowledges to be supported by the specification at paragraph 73, Examples 4, 8, and 9, and by original claims 15-18. The Examiner has not suggested that any of the specific steps recited in claim 46 is lacking in enablement and has acknowledged that, "one may presume that regulatory elements from other *C. elegans* genes encoding secretory products (that, *sic*) would direct expression in a pharyngeal gland cell or amphid sheath cell exist, and the specification describes methods by which one could identify endogenous secretory products that are secreted from a pharyngeal gland cell or amphid sheath cell in *C. elegans* or the analogous organs in other nematodes." (office action of 4/6/05, page 5). The Examiner has further acknowledged that the specification teaches methods for isolating

regulatory elements for use in making the claimed invention (office action of 4/6/05, pages 12 and 15). The Examiner has also acknowledged (with respect to *vap-1*) that given a genomic fragment that contains a minimal regulatory sequence it would be routine in the art to narrow down or determine the minimal sequence, if desired (office action of 4/6/05, page 19). Applicants submit that similar methods could be used for other genes encoding secretory products. Withdrawal of the rejection of claim 46 and claims dependent therefrom is respectfully requested.

The Office Action states that claims 114-119 and 122-129 are rejected for reasons of record set forth in the Office Action of 3/23/04. Claims 114 and 119 have been canceled. Claim 115 as amended recites a method of generating a transgenic *C. elegans* nematode comprising steps of: (a) selecting a parasitic nematode secretory protein that is expressed in a pharyngeal gland cell or an amphidial gland cell of a parasitic nematode; (b) identifying a *C. elegans* homolog of the protein selected in step (a); and (c) generating a transgenic *C. elegans* nematode, wherein cells of the transgenic nematode comprise a DNA element encoding a detectable marker operably linked to a regulatory sequence of the gene that encodes the *C. elegans* homolog. Neither Office Action suggests that there is a lack of enablement for step (a) or (b) or that there is a lack of enablement for generating a transgenic *C. elegans* nematode. As noted above, the instant Office Action acknowledges that the specification provides methods for identifying regulatory sequences required by the claims. Withdrawal of the rejection of claim 115 and claims dependent therefrom is respectfully requested.

Claim 124 as amended recites a method of generating a transgenic *C. elegans* nematode comprising steps of: (a) selecting a *C. elegans* secretory protein that is expressed in a pharyngeal gland cell or an amphid sheath cell; and (b) generating a transgenic *C. elegans* nematode, wherein cells of the transgenic nematode comprise a transgene comprising a DNA element that encodes a detectable marker operably linked to a regulatory sequence of the gene that encodes the *C. elegans* secretory protein. Applicants note that the Examiner has indicated in the instant Office Action that “one may presume that regulatory elements from other *C. elegans* genes encoding secretory products (that, *sic*) would direct expression in a pharyngeal gland cell or amphid sheath cell exist, and the specification describes methods by which one could identify endogenous secretory products that are secreted from a pharyngeal gland cell or amphid sheath cell in *C. elegans* or the analogous organs in other nematodes.”. The Examiner has also acknowledged that the specification provides methods for identifying regulatory elements

required by the claims. Withdrawal of the rejection of claim 124 and claims dependent therefrom is respectfully requested.

Rejections under 35 U.S.C. § 102

Claims 125-128 are rejected as being anticipated by Plenefisch, et al., for reasons of record. The Examiner notes that the claims do not require expression in any particular type of cell. These claims have been amended to depend on claim 124, which recites a *C. elegans* secretory protein that is expressed in a pharyngeal gland cell or an amphid sheath cell. Withdrawal of the rejection is respectfully requested.

Additional claim amendments and new claim

Claim 47 has been amended to recite the parasitic nematode is a member of an order selected from the group consisting of the Strongylida, Rhabditida, Ascaridida, Spirurida, Oxyurida, Enoplida, Tylenchida, or Dorylaimida nematode orders. Support for the amendment is found in original claim 16.

New claim 143 is dependent on claim 46 and recites that the parasitic nematode is a member of a genus selected from the list consisting of the Haemonchus, Oestertagia, Trichostrongylus, Cooperia, Dictyocaulus, Strongylus, Oesophagostomum, Syngamus, Nematodirus, Heligmosomoides, Nippostrongylus, Metastrongylus, Angiostrongylus, Ancylostoma, Necator, Uncinaria, Bunostomum, Strongyloides, Steinernema, Ascaris, Parascaris, Toxocara, Toxascaris, Baylisascaris, Anisakis, Pseudoterranova, Heterakis, Wuchereria, Brugia, Onchocerca, Dirofilaria, Loa, Thelazia, Dracunculus, Gnathostoma, Enterobius, Oxyuris, Syphacia, Trichinella, Trichuris, Capillaria, Globodera, Heterodera, Meloidogyne, Anguina, Ditylenchus, Hirschmanniella, Naccobus, Pratylenchus, Radopholus, Criconema, Tylenchulus, Paratylenchus, Aphelenchus, Bursaphelenchus, Longidorus, Xiphinema, Trichodorus, and Paratrichodorus nematode genera. Support for the amendment is found in original claim 17.

In conclusion, in view of the amendments and remarks presented herein, the application and pending claims comply with the requirements of 35 U.S.C. §112 and 35 U.S.C. §102. Applicants therefore respectfully submit that the present case is in condition for allowance. A Notice to that effect is respectfully requested.

If, at any time, it appears that a phone discussion would be helpful in resolving any remaining issues, the undersigned would greatly appreciate the opportunity to discuss such issues at the Examiner's convenience. The undersigned can be contacted at (617) 248-5000 or (617) 248-5071 (direct dial).

Please charge the fee for a one month extension of time to our Deposit Account No. 03-1721. Please charge any additional fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully submitted,

A handwritten signature in cursive script, reading "Monica R. Gerber".

Monica R. Gerber
Registration Number 46,724

Date: July 28, 2005

Choate, Hall & Stewart, LLP
Exchange Place
53 State Street
Boston, MA 02109
(617) 248-5000

3953358_1.DOC